

Case Report Rapport de cas

Renal nephroblastoma in a 3-month-old golden retriever

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Abstract — Nephrectomy was performed in a 3-month-old intact female golden retriever dog for a renal nephroblastoma. The dog has remained disease-free for 19 months with nephrectomy alone. The adoption of human Wilms' tumor grading criteria may be useful in determining clinical stage, adjuvant treatment options, and prognosis in this rare disease.

Résumé — Néphroblastome rénal chez un Golden Retriever âgé de 3 mois. Une néphrectomie a été réalisée sur une chienne Golden Retriever intacte âgée de 3 mois pour un néphroblastome rénal. La chienne est demeurée exempte de maladie pendant 19 mois, seulement à l'aide de la néphrectomie. L'adoption du critère humain de Wilms pour la classification des tumeurs peut être utile pour déterminer le stade clinique, les options de traitement auxiliaire et le pronostic de cette maladie rare.

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Nephroblastoma is a rare tumor and is most often found in juvenile dogs (1). It is a malignancy that arises from the embryonic remnants of the immature kidney (2). In humans, nephroblastoma is the most common primary malignant renal tumor of children (2). In all previous reports of renal nephroblastoma in puppies less than 1 y of age, treatment with surgery alone or with surgery and adjuvant chemotherapy did not prevent progression of disease and death (3–5). This is the first case report of a puppy this young with nephroblastoma, with the longest reported survival time without adjuvant treatment. The present report shows that a puppy, with renal nephroblastoma Stage II with favorable histopathology, may survive over 19 mo with nephrectomy alone. The adoption of the human Wilms' tumor grading system in canine nephroblastoma may be useful in determining clinical stage, adjuvant treatment options, and prognosis in this rare disease.

Case description

A 3-month old, intact female golden retriever dog was presented to the Ontario Veterinary College (OVC) Teaching Hospital for assessment, diagnosis, and treatment of an abdominal mass. The primary care veterinarian initially evaluated the dog with

routine physical examination during vaccination. An abdominal mass was palpated in the left mid-abdomen. The dog was re-evaluated 5 d later and the abdominal mass was larger and could be visualized protruding from the abdomen on the left side, just caudal to the last rib. The owner did not report any clinical signs associated with the mass. An abdominal ultrasound performed by the primary care veterinarian showed a cavitated soft tissue mass on the medial aspect of the left kidney. The patient was referred to the OVC Teaching Hospital for further evaluation and treatment of the left renal mass.

On presentation, the dog was quiet for a 3-month-old puppy, but alert, with a body weight of 9.6 kg. Vital parameters were within normal limits. On physical examination a large, nonpainful intra-abdominal mass was visible and palpable in the left cranial abdomen. The rest of the examination was unremarkable. A complete blood (cell) count (CBC) showed a mild elevation of the white blood cell (WBC) $22.1 \times 10^9/L$, [reference interval (RI): 4.9 to $15.4 \times 10^9/L$], with an increased segmented neutrophil count ($12.38 \times 10^9/L$; RI: 2.9 to $10.69 \times 10^9/L$), lymphocyte count ($7.51 \times 10^9/L$; RI: 0.8 to $5.1 \times 10^9/L$), and monocyte count ($1.77 \times 10^9/L$; RI: 0 to $1.1 \times 10^9/L$). Serum biochemistry profile, prothrombin time, partial thromboplastin time, and urinalysis were unremarkable. Blood typing was DEA 1.1 positive.

The dog was placed under general anesthesia for computed tomography (CT) examination of the abdomen and thorax, which showed a large left kidney mass ($13 \times 9 \times 7.4$ cm) characterized by mixed fluid and soft tissue density with mild peripheral contrast enhancement. The mass had a decreased radiodensity compared with the normal renal parenchyma. The thorax was normal on CT scan. An ultrasound-guided fine-needle aspirate of the left renal mass was obtained without complication following the CT scan. The dog recovered uneventfully. The cytological interpretation was consistent

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Figure 1. Intraoperative image of the dog during exploratory laparotomy. The head of the patient is to the right of the picture. Note the kidney mass (star), caudal kidney pole (arrowhead) and the enlarged renal vein (arrow).

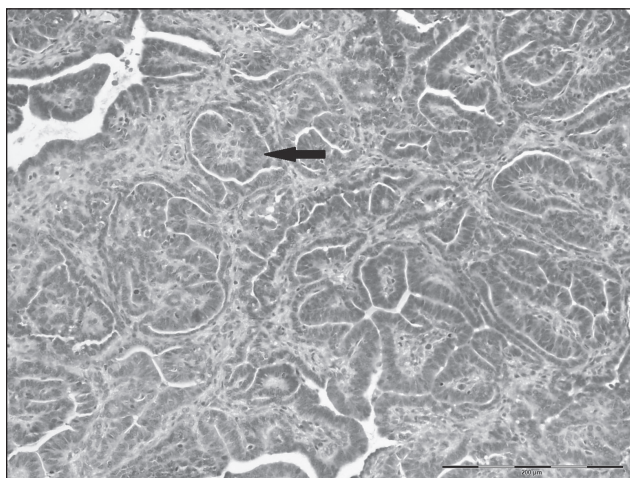


Figure 2. Section of the renal mass. There are numerous tubules lined by well-differentiated columnar epithelial cells as well as occasional glomeruloid-like structures (arrow). (Hematoxylin & eosin, bar = 200 µm)

with renal nephroblastoma with moderate non-suppurative inflammation.

The following day, an exploratory laparotomy was performed. Abnormal findings on exploratory laparotomy included: the large left renal mass with extension and adhesion of the tumor to the left ovary and left uterine horn and an enlarged mesenteric lymph node. Ovariohysterectomy was performed during left nephrectomy due to involvement of the uterus and left ovary with the tumor. The left renal mass was dissected bluntly from the retroperitoneum. Peritumoral vessels were ligated with surgical clips (Premium Surgiclip II M-975; Auto Suture, Covidien, St. Laurent, Quebec) or managed with electrocautery. The renal arteries were visualized and ligated with 2 figure-of-eight transfixation ligatures of 2-0 monofilament polydioxanone suture. The renal vein was severely enlarged and was approximately the size of the caudal vena cava at this level (Figure 1). It was ligated in the same manner as the renal arteries. The renal mass was removed en bloc with both ovaries

Table 1. Humans' Wilms' tumor (nephroblastoma) grading^a

Stage I	Tumor confined to the kidney, completely removed without rupture; vessels of the renal sinus are not involved; no tumor evidence at or beyond the margins of resection
Stage II	Tumor extends beyond the kidney but is completely excised without tumor evidence at or beyond the margins of resection
Stage III	Tumor not completely excised with extension confined to the abdomen
Stage IV	Hematogenous metastasis or metastasis to distant lymph nodes outside the abdominopelvic region
Stage V	Bilateral kidney involvement at the time of diagnosis
Histopathological classification	Favorable: no evidence of anaplasia Unfavorable: evidence of anaplasia or a sarcomatous component

^a From National Wilms' Tumor Study Group (NWTSG) Staging System for Renal Tumors (3).

and the uterus. The enlarged mesenteric lymph node was extirpated during surgery. The abdomen was lavaged with copious amounts of sterile physiologic saline. A 6-inch pain-diffusion catheter (Mila diffusion/wound radio-opaque catheter, Mila International, Erlanger, Kentucky, USA) was placed in the subcutaneous layer and Bupivacaine (Bupivacaine hydrochloride, 0.5%; Hospira Healthcare, Montreal, Quebec), 1.5 mg/kg body weight (BW), was administered post-operatively. The dog recovered uneventfully from anesthesia. Postoperative treatments included maintenance intravenous fluid therapy (Plasma Lyte A; Baxter, Mississauga) 2 mL/kg BW per hour for 36 h, fentanyl (Fentanyl citrate 50 µg/mL, Chiron Compounding Pharmacy, Guelph, Ontario) continuous rate infusion, 2 to 6 µg/kg BW/h, IV, for 24 h, cefazolin (Cefazolin; Apotex, Toronto, Ontario), 22 mg/kg BW, IV, q8h, for 24 h, and bupivacaine (Hospira Healthcare), 1 mg/kg BW, q6h for 36 h, via pain diffusion catheter. The patient was discharged 48 h after surgery with oral tramadol (Tramadol Hcl; Chiron Compounding Pharmacy), 20 mg, q8h, orally for 5 d. The renal mass, ovaries, uterus, and mesenteric lymph node were submitted for histopathology. The histological diagnosis of the renal mass was kidney nephroblastoma (Figure 2), with a normal ovary, uterus, and a reactive mesenteric lymph node.

The dog returned 14 d after surgery for suture removal. The dog was subjectively more responsive and active than she had been before surgery, with a body weight of 11 kg. Physical examination and vital parameters were normal. Adjunctive chemotherapy with vincristine sulfate, actinomycin D, and doxorubicin was recommended to the owner but was declined. Five weeks after surgery the dog was re-checked and appeared to be growing well, with a body weight of 16 kg. Staging was performed with an abdominal ultrasound and 3-view thoracic radiographs and no metastatic disease was detected. The owner again declined adjunctive treatment and further re-staging. Follow-up by telephone 4, 7, 11, and 19 months after surgery, found that the dog was doing very well at home with no health concerns.

Table 2. Summary of reports of canine renal nephroblastoma in the veterinary literature

Primary author (reference)	Number of cases	Age	Breed	Gender	Chemotherapy protocol	DFI (months)	MST (months)
Montinaro (Current case report)	1	3 mo	Golden retriever	F	None	> 17	> 19
Bryan (3)	5	1–12 y (mean 5.2 y)	NA	2 M 1 MC 2 FS	None	NA	0–6 (median 6 mo)
Seaman (9)	1	8 y	Labrador retriever	MC	Vincristine and doxorubicin	25	25
Frimberger (4)	1	4 mo	Bernese mountain dog	F	Vincristine, doxorubicin, actinomycin D	3.75	4
Caywood (10)	1	2 y	Mixed breed	FS	Actinomycin D	8.5	15
Coleman (5)	1	8 mo	Beagle	F	None	1.5	NA

M — male, F — female, MC — male castrated, FS — female spayed. DFI — disease free interval; MST — median survival time; NA — not available.

Discussion

Primary renal neoplasia is rare in dogs, with a reported incidence of 0.6%. The majority of renal tumors reported in dogs are carcinomas (6). Nephroblastoma is a rare tumor that tends to be diagnosed in juvenile dogs (1). In humans, nephroblastoma is also referred to as Wilms' tumor and it is the most common primary malignant renal tumor of children (2). Staging criteria for Wilms' tumor in humans depends on the anatomic tumor extension and metastasis. These staging criteria have been described by the National Wilms' Tumor Study Group (7). Staging of Wilms' tumor is divided into 5 stages and classified based on favorable or aggressive histopathology (6) (Table 1). In humans, renal nephroblastoma is treated by nephrectomy, unless there is bilateral renal involvement. Chemotherapy and/or radiotherapy may or may not be used as adjunctive treatment, depending on the histopathological characteristics and tumor stage (8). Chemotherapy with vincristine and actinomycin D is typically recommended in humans for disease that is stage II or higher (5). Intra-abdominal radiotherapy is performed in Stage III tumors when there is the potential for microscopic or macroscopic disease at the surgery site (5). The Wilms' tumor staging scheme is commonly used in humans and, considering that canine nephroblastomas are so rare, this may serve as a way to classify this disease in dogs and help prognosticate and make treatment plans.

Canine renal nephroblastoma has been reported in the veterinary literature in a total of 9 cases. The dogs in these reports range in age from 4 mo to 12 y (3–5,9,10). A summary of the reported cases of canine nephroblastoma is presented in Table 2. Bryan et al (3) reported 5 cases of nephroblastoma in a retrospective study of primary renal neoplasia in dogs. Three of the 5 dogs were less than 2 years old. The mean age was 5.2 y (range of 1 to 12 y) with a median survival time of 6 mo. Of the 5 dogs reported with nephroblastoma in this series, 1 had metastasis at the time of diagnosis and 3 of the remaining 4 had evidence of metastatic disease at the time of death (3).

A single case report by Seaman and Patton (9) describes an 8-year-old dog with nephroblastoma that was treated with unilateral nephrectomy, vincristine, and doxorubicin. That dog would be classified as having stage I disease with unfavorable histopathology using the human Wilms' tumor classification, due to the presence of a sarcomatous component reported. The dog had a disease-free period for more than 25 mo and a survival time of > 25 mo (9). Frimberg et al (4) reported a 4-month-old dog with a renal nephroblastoma that would be considered stage III with favorable histopathology using the human Wilms' tumor classification. That dog was treated with nephrectomy followed by vincristine, actinomycin D, and doxorubicin. Sixteen weeks after surgery the dog was euthanized for metastatic disease involving lungs, liver, intra-abdominal lymph nodes, and the retroperitoneal space (4).

Other single case reports of canine renal nephroblastoma in the veterinary literature include a 2-year-old dog, that would be considered a stage II Wilms' tumor with unfavorable histopathology. That dog was treated with nephrectomy, actinomycin D, and intra-abdominal radiotherapy and had metastasis within 8.5 mo and was euthanized 15 mo post diagnosis (10). An 8-month-old dog, considered a stage II Wilms' tumor with unfavorable histopathology, was treated with surgery alone and developed metastasis within 6 wk post-surgery (5).

Nephroblastoma can also occur in extrarenal locations in dogs and humans. Renal and spinal nephroblastoma are similar histopathologically in dogs (11). Primary spinal cord nephroblastoma has been reported in dogs (12). Usually nephroblastomas occur as intradural, extramedullary masses, but they can also occur as intramedullary or extradural lesion in dogs (12–17). Long-term survival has been reported with surgical cytoreduction and radiotherapy in dogs with canine spinal cord nephroblastoma (17).

In the case reported here, this dog was considered to have stage II disease with favorable histology, based on the human grading for Wilms' tumor (Table 1), because the tumor extended beyond the kidney but was completely removed. The left ovary

and uterus were involved with the renal mass and the entire uterus and both ovaries were removed en-bloc to achieve complete excision of the mass. There was no histopathologic evidence of tumor infiltration into the adjacent uterus and ovary.

An enlarged renal vein was also visualized during the exploratory celiotomy, which is also consistent with stage II disease. This finding may have been due to venous stasis from the compression of the mass or to the tumor involvement but subsequently no macroscopic involvement of the renal sinus was found on histology. The histopathology was characterized by well-differentiated epithelial cells with no signs of anaplasia, compatible with a favorable histology (Figure 2).

In humans it has been shown that tumors that are composed of well-differentiated tubular and glomerular structures have been associated with a good prognosis, whereas anaplasia and sarcomatous stroma have been associated with metastasis and poor prognosis (18). The recommendation for this case was to follow surgery with adjunctive chemotherapy. The proposed protocol was vincristine sulfate, actinomycin D, and doxorubicin. This protocol was based on the available information on adjuvant treatment for this disease, which is sparse. There were some concerns about the administration of chemotherapy to a puppy this young. Information regarding the risks associated with chemotherapy administration in puppies is not confirmed in the literature. There are only 2 reports of adjunctive treatment of nephroblastoma in dogs less than 1 year of age. The disease-free intervals in both cases were short at 6 and 15 wk; survival time was available only for the latter case and was 16 wk (4,5).

To the authors' knowledge there are no reports of renal nephroblastoma in a 3-month-old puppy with stage II disease and favorable histology treated with nephrectomy alone resulting in a relatively long survival time of > 19 mo post-operatively without any adjunctive treatment. A full physical examination in puppies before vaccination is very important to identify congenital disease or other significant health problems. This case highlights the benefits of a full physical examination, even with an apparently healthy puppy, and the importance of good teamwork between the primary care veterinarian and veterinary specialist to achieve diagnosis and treatment in a short period of time and a positive outcome. The adoption of the human Wilms' tumor grading criteria in veterinary medicine may help

to guide the appropriate treatment course with this rare disease in dogs. This case report demonstrates that it is possible for a dog with stage II renal nephroblastoma with favorable histology to survive over 19 mo with nephrectomy alone.

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